

CLAIMS

1. A process for preparing a tripeptide, including a salt thereof, of the formula (I)

5

Ac-D-2Nal-D-4ClPhe-D-3Pal-OH (I)

or (IX)

10 Boc-D-2Nal-D-4ClPhe-D-3Pal-OH (IX),

comprising the following consecutive steps for the preparation of (I):

(a) Reacting Boc-D-4ClPhe-OH with HONSu to form
15 Boc-D-4ClPhe-OSu (VII);

(b) Reacting Boc-D-4ClPhe-OSu (VII) with H-D-3Pal-OH to form Boc-D-4ClPhe-D-3Pal-OH (VIII);

(c) Reacting Boc-D-4ClPhe-D-3Pal-OH (VIII) with Boc-D-2Nal-OSu prepared by reacting Boc-D-2Nal-OH with HONSu to form
20 Boc-D-2Nal-D-4ClPhe-D-3Pal-OH (IX);

(d) Reacting Boc-D-2Nal-D-4ClPhe-D-3Pal-OH (IX) with acetic acid to form Ac-D-2Nal-4ClPhe-D-3Pal-OH (I);

or the consecutive steps (a) through (c) for the preparation of (IX).

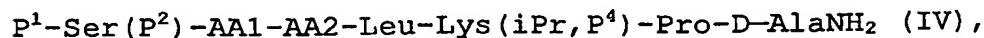
25

2. The tripeptide Ac-D-2Nal-D-4ClPhe-D-3Pal-OH (I) or a salt thereof.

3. The tripeptide Boc-D-2Nal-D-4ClPhe-D-3Pal-OH (IX) or a
30 salt thereof.

4. A process for preparing an LHRH antagonist or a pharmaceutically acceptable salt thereof, comprising coupling

a tripeptide Ac-D-2Nal-D-4ClPhe-D-3Pal-OH (I) with a heptapeptide (IV) of the general formula

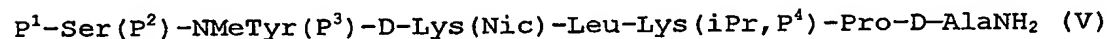


5

wherein P^1 is selected from H or amino protecting group, P^2 is H or OH-protecting group, P^4 is H or an amino protecting group such as Boc, AA1 is natural or synthetic amino acid and AA2 is natural or synthetic amino acid or zero.

10

5. The process of claim 4, wherein the heptapeptide of the general formula (IV) is a heptapeptide of the general formula

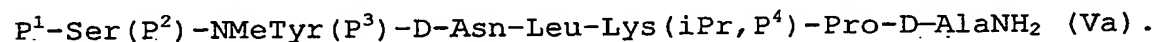


15

wherein P^3 is H or -OH protecting group.

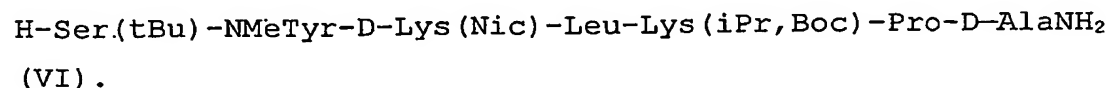
6. The process of claim 4, wherein the heptapeptide of the general formula (IV) is a heptapeptide of the general formula

20



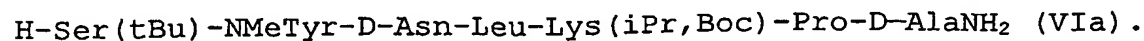
wherein P^3 is H or -OH protecting group.

25 7. The process of claim 5, wherein the heptapeptide of the general formula (V) is a heptapeptide of the formula



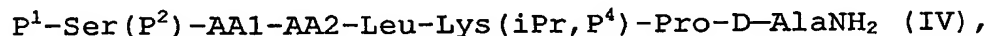
30

8. The process of claim 6, wherein the heptapeptide of the formula (VI) is a heptapeptide of the formula



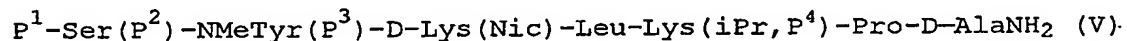
9. A process for preparing an LHRH antagonist or a pharmaceutically acceptable salt thereof, comprising coupling the tripeptide Boc-D-2Nal-D-4ClPhe-D-3Pal-OH (IX)

5 with a heptapeptide (IV) of the general formula



wherein P^1 is selected from H or amino protecting group, P^2 is
10 H or OH-protecting group, P^4 is H or amino protecting group such as Boc, AA1 is a natural or synthetic amino acid and AA2 is a natural or synthetic amino acid or zero.

10. The process of claim 9, wherein the heptapeptide of the
15 general formula (IV) is a heptapeptide (V) of the general formula



20 wherein P^3 is H or OH-protecting group.

11. The process of claim 10, wherein the heptapeptide of the general formula (V) is the heptapeptide

25 H-Ser(tBu)-NMeTyr-D-Lys(Nic)-Leu-Lys(iPr, Boc)-Pro-D-AlaNH₂ (VI).

12. The process of claim 9, wherein the heptapeptide of the general formula (IV) is a heptapeptide of the general formula

30 $P^1\text{-Ser}(P^2)\text{-NMeTyr}(P^3)\text{-D-Asn-Leu-Lys}(i\text{Pr}, P^4)\text{-Pro-D-AlaNH}_2 \text{ (Va)},$

followed by substituting the Boc group by an acyl group, in particular an acetyl group.

13. The process of claim 12, wherein the heptapeptide of the general formula (IV) is the heptapeptide

H-Ser(tBu)-NMeTyr-D-Asn-Leu-Lys(iPr,Boc)-Pro-D-AlaNH₂ (VIa),

5

followed by substituting the N-terminal Boc group by an acyl group, in particular an acetyl group.